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| APPLICATION NO.               | FILING DATE | FIRST NAMED INVENTOR  | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-------------------------------|-------------|-----------------------|---------------------|------------------|
| 10/700,107                    | 11/03/2003  | Steven P. Schwendeman | 22727/04196         | 5145             |
| 24024                         | 7590        | 06/01/2006            | EXAMINER            |                  |
| CALFEE HALTER & GRISWOLD, LLP |             |                       | FUBARA, BLESSING M  |                  |
| 800 SUPERIOR AVENUE           |             |                       | ART UNIT            | PAPER NUMBER     |
| SUITE 1400                    |             |                       |                     |                  |
| CLEVELAND, OH 44114           |             |                       | 1618                |                  |

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/700,107             | SCHWENDEMAN ET AL.  |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Blessing M. Fubara     | 1618                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 13 March 2006.

2a) This action is FINAL.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-7 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-7 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

|  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                     | Paper No(s)/Mail Date. _____ .  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____ .                                  |

## **DETAILED ACTION**

Examiner acknowledges receipt of request for continued examination under 37 CFR 1.114, request for extension of time, amendment and remarks, all filed 3/13/2006. Claim 1 is currently amended and claims 1-7 are pending. Claims 8-25 were canceled in the preliminary amendment filed 11/03/2003.

### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cleland et al. (US 5,643,605).

Cleland discloses compositions and methods for encapsulating adjuvants or biologically active agents in microsphere compositions (abstract, column 1, lines 8-10 and column 3, lines 1-9). The composition comprises PLGA microspheres encapsulating adjuvants (column 3, lines 18-20). The ratio of lactide to glycolide is from 100:0 to 0-100 weight percent (column 3, lines 22-23 and claim 1). The microspheres have a median diameter of 20-100 $\mu$ m (column 3, lines 25-27); adjuvants, which are biologically active agents, are released in a triphasic pattern (column 3, lines 44-52); and the viscosity of the PLGA polymers is 0.1 to 1.2 dL/g (column 3, lines 40 and 58). Cleland further teaches a method for encapsulating the adjuvants in the PLGA microspheres. The method comprises dissolving PLGA in an organic solvent to produce a solution, adding adjuvant to the solution to produce PLGA-adjuvant mixture, adding the mixture

to an emulsification bath to produce microspheres comprising second emulsion and hardening the microspheres to produce hardened microspheres comprising encapsulated adjuvants (column 3, line 64 to column 4 line 8). The formulation further comprises carriers and the carriers used in the prior art are those described in Remington's Pharmaceutical Sciences, 16<sup>th</sup> edition, 1980, (column 7, lines 4-10). Specifically, Cleland teaches that the formulation comprises preservatives, buffer or buffers, polyethylene glycol, mannitol and poloxamer non-ionic surfactant (column 9, lines 24-34). The pH of the formulation ranges from about 5-8 (column 9, lines 35-40). Cleland discloses proteins as adjuvants (column 9, lines 59-67). Cleland teaches that various molecular weights and lactide to glycolide ratios of PLGA used. The molecular weight of the PLGA ranges from 12 kDa to 100 kDa and that ratio of lactide to glycolide ranges from 50:50 to 75:25 (column 10, lines 2-5).

The polyethylene glycols and the poloxamer surfactants of the prior art are referenced as known and available on the market and therefore, have known molecular weights. But since the molecular weights recited in the application do not have units, a comparison of molecular weights cannot be made. It is thus assumed that the molecular weight of polyethylene glycols and poloxamer of the prior art is comparable to the claimed molecular weights. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Cleland. One having ordinary skill in the art would have been motivated to prepare the PLGA composition of Cleland according to the method taught in Cleland. Although Cleland is silent on the molecular weight of the polyethylene glycols and poloxamer, one having ordinary skill in the art would know to use polyethylene glycol and poloxamer of specified molecular since the polyethylene glycol and poloxamer are known and marketed (column 9, lines

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25-30). In the absence of a showing the recited molecular weights of polyethylene glycol and poloxamer are not critical over the prior art.

***Response to Arguments***

1. Applicant's arguments filed 3/13/06 have been fully considered but they are not persuasive.

***Use of the PEG or Poloxamer in Cleland vs. applicant's purpose***

Although Cleland does not disclose that the PEG or Poloxamer is used as pore former, it is noted that the pore forming ability of the PEG or Poloxamer flows from the properties of these polymers. Therefore, if the PEG or poloxamer is acting as a pore forming agent in applicants' invention, then the same PEG or poloxamer would also act as a pore former in the prior art even if the art has not described the PEG or poloxamer as such. PEG or Poloxamer as pore forming agent as recited by applicants, or PEG/Poloxamer as stabilizer for protein as in the prior art, are functions of the PEG or Poloxamer flowing from the property of the PEG or Poloxamer. Also, one of the steps in the instant invention is a lyophilization step, which is also noted and admitted by applicants to be one of the Cleland steps.

***10-30% (w/w) in claimed invention vs. 0.1-30% (w/w)***

The amount of 0.1-30% of the prior art overlaps the 10-30% in the claimed invention. Specifically, there is at least a point in that continuum of range of 0.1-30% that would intersect with at least a point on the claimed 10-30%. There is no demonstration with factual evidence that the range 10-30% (w/w) in the claimed invention provides unusual/unexpected results knowing that common points are present within each of the ranges of the claimed invention and prior art.

*pH*

Since both the composition of the claimed invention and the prior art contain PEG or Poloxamer and biological agent, it is reasonable to expect that the pH of the microenvironment would be the same for formulations that undergo lyophilization or vacuum drying, during which volatile excipients are expelled at the appropriate temperature and pressure. A pH of 5-8 in the prior art as described above is greater than 3, which is the pH called for by the claims.

**Other Matters: Presentation of Claims**

Claims 8-25 were cancelled by the preliminary amendment filed 11/03/2003. In order to comply with practice of amendment, all claims must be listed with the appropriate status identifiers. In this case claims 8-25 should be listed with the cancelled status identifier as exemplified below:

Claim 1

Claim 7

Claims 8-27 (canceled)

It is hoped that applicants will adopt the format for claim amendment and listing of all claim to avoid holding the amendment as non-compliant

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara  
Patent Examiner  
Tech. Center 1600

